Antitoxine in Diphtheria in Berlin, New York, and in the Municipal Hospital of Philadelphia.

BY

LOUIS FISCHER, M.D.,

INSTRUCTOR IN DISEASES OF CHILDREN AT NEW YORK POST-GRADUATE SCHOOL AND HOSPITAL; PHYSICIAN OF THE MESSIAH HOME FOR CHILDREN; ATTENDING PHYSICIAN TO THE GERMAN POLIKLINIK (CHILDREN'S DEPARTMENT).

FROM

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES,

JANUARY, 1895.

Reprinted from The American Journal of the Medical Sciences, January, 1895.

ANTITOXINE IN DIPHTHERIA IN BERLIN, NEW YORK, AND IN THE MUNICIPAL HOSPITAL OF PHILADELPHIA.

By Louis Fischer, M.D.,

INSTRUCTOR IN DISEASES OF CHILDREN AT NEW YORK POST-GRADUATE SCHOOL AND HOSPITAL; PHYSICIAN OF THE MESSIAH HOME FOR CHILDREN; ATTENDING PHYSICIAN TO THE GERMAN POLIKLINIK (CHILDREN'S DEPARTMENT).

The new therapeutic agent antitoxine has been before us since 1890, when, at the hygienic institute at Berlin, Behring told us of its effects in rendering animals immune in diphtheria. He described the method of injecting small quantities of virulent cultures into the abdominal cavity of guinea-pigs.

It is a well-known fact that guinea-pigs are more sensitive to the action of diphtheritic poison than are other animals, and for this reason they serve the purpose of experimental work better than other animals. Behring modified the action of this virulent diphtheritic bouillon, by previously injecting his animals with iodine trichloride, and found that guinea-pigs could endure larger doses by this method than otherwise.

Behring read a paper in the summer of 1891, at London, before the International Congress of Hygiene and Demography, in which he detailed his methods and results.

Commencing with guinea-pigs, Wernecke then secured immunity in sheep, and Aronson in dogs; then oxen were tried, but yielding very unsatisfactory results were finally abandoned. In order to secure large quantities of serum it was tried on horses, and finding that immunity could be transferred they are at present utilized.

In speaking of serum or antitoxine I invariably refer to that derived from the blood serum of the jugular vein of the horse.

Theory of Immunity. Behring and Ehrlich found that by injecting small quantities of virulent poisons and allowing the animal to recover we could arrive at a certain point which could be called *tolerance* of their specific poison, and this tolerance is called *immunity*. It was further found that this immunity could be conveyed to other animals by injecting certain quantities of serum derived from the blood of immune animals, and this immunity would not only last for some time but would protect the animal against disease from this one toxic agent if injected. Behring found that this immunity applied to tetanus and diphtheria. Ehrlich used vegetable poisons, ricin and abrin, and produced immunity. This being, then, the foundation of serotherapy, it was found that

certain quantities of serum, 0.1 c.c. would protect a guinea-pig weighing 400 gm., or 1 c.c. would protect a guinea-pig weighing 4000 gm. Thus the weight was transferred to human beings and the approximate quantity necessary to render a child immune was thus determined. At present two men are prominent in this work, Behring and Aronson. Both have prepared so-called "Heilserum." Another kind of serum prepared is called "Immunisirungs-Lösung." The former is healing serum, powerful, and is to be applied where diphtheria has already manifested itself. The latter serum is to be used as a prophylactic.

While in Berlin last summer I was permitted to see cases of diphtheria in the *Institut für Infektions-Krankheiten*, through courtesy of Dr. Wasserman—five malignant cases, all of which recovered.

It is proper to state that the so-called Koch's Institute for Infectious Diseases was erected at the time of the tuberculin era, and is still used for this purpose. In this institute Behring's serum only is used. The largest Children's Hospital for Infectious Diseases is under the directorship of Prof. Baginsky—known as the Kaiser und Kaiserin Friedrich Kinderkrankenhaus, where Aronson's serum only has been used.

Extended courtesies by Prof. Baginsky and Dr. Hans Aronson gave me opportunity of acquainting myself with the method and details of antitoxine. I need only refer to statistics given to me by Prof. Baginsky, who stated that, averaging all mild and malignant cases, the mortality was in three years from 1890–93 out of 1081 cases of diphtheria treated 421 deaths, or 38.9 per cent. mortality.

From January 1 to March 14, 1894, there were 86 cases, with 38 deaths, a mortality equal to 41.8 per cent. On March 14th Aronson's antitoxine was first used, and until June 20th there were 128 cases treated with the same remedy—of these 128 cases, 17 died, or a mortality of 13.2 per cent.

Baginsky's statement is well worth repeating, that "We have never had such a low mortality with our mildest epidemics and our best form of treatment."

The following cases treated by me will serve to illustrate how antitoxine was used, and the results:

Case I.—Dora T., aged eleven years, a healthy, well-nourished girl, had been ill about one day. In an adjoining room, a boy, aged fifteen years, was sick with diphtheria. My patient was exposed, and her mother examined her throat and discovered patches. When I first saw her I found the temperature in the axilla $102\frac{3}{5}°$ F. There was intense thirst, general pains in the body, marked malaise, dysphagia, and a headache. Pseudo-membranes covered both right and left tonsils and the posterior pharyngeal wall. I ordered a placebo.

I first made a culture from the throat, the report proved Klebs-Loeffler bacilli, verifying the clinical diagnosis. I then injected 5 c.c. of serum, in the presence of Dr. Gerlach, of the New York Post-Graduate Hospital, with a small hypodermatic syringe, at which injection some serum was

wasted. I then took a better syringe, and injected 5 c.c. of Aronson's serum in the back by pinching a fold of skin between the shoulder-blades. No reaction followed. The next day my patient was greatly improved. Greenish-yellow pseudo-membranes remained about two days following the injection, and on the third day no traces of membranes were visible, although the pharynx and tonsils were still inflamed. On the fourth day no sign of the disease remained, and the little girl was up and hungry. The general malaise seemed to pass off about one day after the injection.

This patient was attacked much more severely than the first child that infected her. A careful examination of the urine was made. Albumin sparingly and an excess of phosphates were present. The trace of albumin also disappeared. No reaction followed the injection of antitoxine.

CASE II.—H. F., aged two years and two months; had never been sick until October 16th; examination by Dr. Berger showed lungs normal; temperature 102° F.; severe inflammation of pharynx and tonsils on both sides. The following day a slight grayish-white pseudo-membrane was visible; the temperature remained 102° F.; the child was apparently very sick.

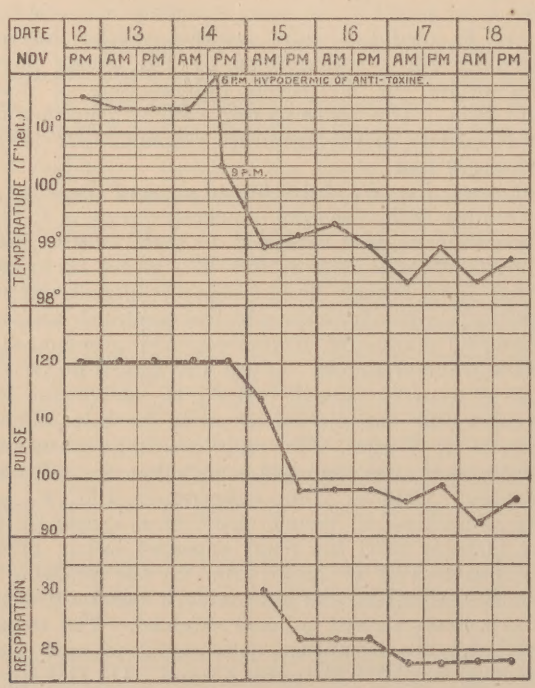
On the following day the child showed signs of dyspnœa; this continued until October 18th, when the temperature rose to 103° F.; cough appeared; pseudo-membrane extended to both tonsils, pharynx, and uvula; evening temperature rose to 104° F.; severe laryngeal stenosis; pulse 140; left lung behind showed sign of dulness. October 19th, child very restless; urgent dyspnœa, which necessitated intubation. The latter was done by Dr. Isaac M. Rottenberg, who pronounced it a septic case and gave a grave prognosis. It was also agreed by Dr. Goldberger that no chance of recovery existed. At 2 P.M., on October 19th, 20 c.c. of Aronson's antitoxine was injected by me in the intra-scapular region in the presence of Dr. Berger. The child seemed to breathe easier after intubation, but passed a restless night. Injection of antitoxine showed no local reaction. October 20th, temperature 103° F., pulse 120; slight dulness on percussion; pseudo-membranes appear the same. On the night of October 20th the child appeared easier; breathing less difficult; temperature 102° F.; pulse 110. On the following day, about forty eight hours after injection of antitoxine, it was decided to extubate, as all grave symptoms seemed to have subsided. The respiration improved hourly, and the membrane commenced to melt away. Temperature (evening) was 101° F., pulse normal. On October 21st there was noticed a few small pinpoint disseminated plaques on pharynx, looking like tonsillitis follicularis in contrast to one huge mass of grayish-white membrane completely hiding the pharynx and tonsils and uvula. On October 22d, temperature and pulse normal, no macroscopic evidence of local disease, and child apparently well and discharged as cured.

This is the most striking case of all, and astounded the attending physicians, as this case was considered hopeless and beyond medical control.

CASE III.—Child; he was seen in consultation with Dr. S. Cohn. Diagnosis, laryngeal croup (diphtheritic). The usual harsh, ringing, croupy cough was distinctly noticeable, and it appeared that unless intubation was rapidly performed asphyxia might result. At midnight 10 c.c. of Aronson's serum was injected by me into the intra-scapular

region. This was not followed by any local reaction. Child improved gradually, and although no further medication was used, was reported well on the second day. This was one of the worst cases, for the laryngeal symptoms were well marked, besides the elevated temperature.

Case IV.—F. V., aged six-and-a-half years, predisposed to catarrhal tonsillitis; taken sick November 11th. Mother discovered white deposit on tonsils. Sent for Dr. Valentine on November 12th. Examination showed that right tonsil was completely covered with a thick membranous deposit, and also a long narrow deposit on the mucous membrane covering palato-pharyngeus muscle behind left tonsil, which moved up and down with it. The post-nasal cavities were plugged. Axillary temperature, 101.4° F., pulse 120.



November 13th. Both tonsils more swollen; left one also well covered with membranous deposit. Discharge from nose thick, tenacious, and profuse. Pain in right ear, back of neck, and back of head. Child drowsy. A. M. temperature 101.4°; pulse 120, P. M. 101.6°; pulse 120.

16th. Attempted to pull membrane off with forceps, which latter slipped, and bleeding resulted. Extension on anterior fauces in front of left tonsil, and in front of uvula. Nares absolutely occluded.

I saw the case about 6 P. M. and injected 20 c.c. of antitoxine of the strength of 1000 antitoxine normal units, in the presence of the nurse and Dr. Valentine. The injection was thrown deeply into the connective tissue of the inter-scapular region to the left of the spine. Temperature at time of injection, 102°; pulse, 120, at 6 P. M. At 9 P. M.

of same evening, three hours later, temperature fell to 100.4°; pulse, 114. Extension of membrane to roof of mouth upward from left tonsil about an inch long and three-quarters of an inch broad. The cervical glands swollen on left side. Bloody mucus from left nostril. All former medication stopped and nurse directed to swab the throat hourly with a 1:2000 bichloride of mercury solution. The new membrane discovered in the morning looked shrunken, and there was no fresh deposit. Right tonsil less swollen. 5 A. M. Temperture, 99°; pulse, 100. No new membrane in throat, but continual shrinkage in size and thickness. Pulse weak and irregular. Stimulants hourly. The membrane melting, and the tonsils assuming normal shape and size; the swelling of cervical glands lessened. Patient feeling well. Nourishment every two hours, succeeded by teaspoonful of *bovinine*. Stimulants hourly, from Thursday morning until Saturday morning. Nasal irrigation was done every three hours, with lukewarm normal saline solution. Two immense plugs of membrane were discharged from nose. The nasal passages remained clear. Treatment was continued by Dr. Valentine.

The diagnosis in all cases was confirmed by a bacteriological culture made by removing a small particle of membrane from portion which appeared oldest, and stroking over agar-agar or blood-serum, and placing in the thermostat. In some instances I submitted inoculations to other bacteriologists and sent cultures to New York Health Department.[1]

CASE V.—A. H., aged nine years, first complained of being unwell Saturday, October 6th; general malaise, feverish and debilitated, loss of appetite, disposed to keep the recumbent posture. Was first seen Sunday morning October 7th. Debility extreme. Skin hot and dry. Temperature 102°. Pulse 120. Coated tongue, foul breath, and examination showed a mass of exudation which completely filled the fauces; nasal breathing obstructed. Diphtheria of a low type diagnosticated. Put upon the bichloride $\frac{1}{4\,0}$ and tinc. ferri chl. ♏v, every three hours, and throat sprayed hourly with weak solution of chloride, and for nourishment whiskey punch freely. Made culture and forwarded to Board of Health. Secured five grammes of antitoxine and gave the whole amount in one injection between shoulder-blades. This was accomplished at 7 P.M. Sunday, when the disease had been present at least forty-eight hours, possibly seventy-two hours, in view of the extent of surface involved by the exudate, although no attention was called to the throat until the morning of the day that the antitoxine was used. No reaction followed the injection. Patient passed a feverish, restless night, and was found no better Monday morning. Report on culture from Board of Health, "true diphtheria." Cadaveric odor from throat almost intolerable. Heart action weak and debility even more pronounced than on previous day. Temperature 100.5° to 102°. Pulse feeble, 120. Positively refuses to take stimulant in any form by mouth. Condition of throat makes deglutition difficult. Appearance of exudate about the same as at the time of the injection the night before. Directed continuance of bichloride treatment and was hourly rubbed and bathed in hot

[1] To Miss Philipps, the nurse in charge of this case, I am greatly indebted for the accurate report, and for temperature, pulse and respiration charts.

brandy, keeping hot brandied cloths to bowels continuously. Monday evening no progress noted and the case assuming a grave aspect. Prognosis unfavorable. New remedy considered inert.

Tuesday morning (thirty-six hours after the use of antitoxine) evident change for the better. Temperature steadily falling. Pulse stronger. Tongue cleaner. Exudate loosening at edges, and surrounding parts look bright and healthy. Improvement continued through the day. Free flow of saliva and mucus from throat, but no membrane exfoliated. It appears thinner and is evidently melting. More comfortable night and evidences of gain in every way.

Wednesday morning. Temperature nearly normal. Pulse 86. Odor from throat nearly gone and membrane rapidly disappearing. Can see underlying surface, and whole appearance is fresh and healthy. No masses or flakes of membrane were loosened or coughed up. It all appears to be melting away.

Thursday. Temperature touched normal. Pulse 86. Throat nearly clear. Nasal passages much freer. Patient declares himself well, and his general tone is excellent. Hungry and calling for solids. Urine examined and found free from albumin.

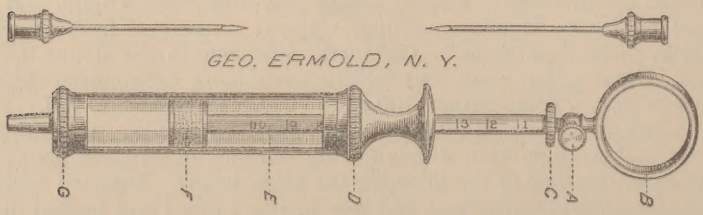
Friday. All visible throat free from exudate. Tongue slightly coated, but moist on edges. Breath entirely free from odor. Temperature 97.5° to 99°. Report on culture taken on Thursday, Loeffler's bacilli still present.

Saturday. Child to all appearances well. Throat normal. Nasal passages open. No evidence of the disease about him. Temperature averaging normal.

Sunday. One week from the use of the antitoxine. Would declare the child quite well, but find report on culture reads, bacilli still present. Kept child quarantined and in bed for ensuing week, and on eleventh day sent culture to the laboratories of both New York and Brooklyn Boards of Health to secure comparative tests. Reports from both read, bacilli present. Persistent nutrition kept up and throat sprayed with Seiler's solution and the bichloride alternately.

Seventeenth day. Sent another culture, and same report is returned. Have not detected any evidence of the disease since Saturday, October 13th, six days after hypodermatic was given, but culture made on 23d inst. still shows characteristic bacilli, and this return was made on every culture until the twenty-first day, when the Board of Health declared them absent. No albumin found save on eighth day, and then only a trace.

(The last case is published by permission of Dr. Catlin, of Brooklyn.)



The syringe used consists of an ordinary glass barrel like any ordinary aspirating syringe, but the fittings are made with asbestos and

linoleum. I have tried to do away with the linoleum, and have had Mr. Ermold construct the syringe of asbestos only. It can easily be sterilized by boiling. The syringe holds about 10 c.cm. or enough for one hypodermatic injection of antitoxine. The calibre of the needles is very large owing to the thick consistence of the serum.

In looking over my list of cases I find that the most instructive were Case V., in consultation with Dr. Catlin, of Brooklyn, Case II., in consultation with Dr. Berger, of New York, and Case IV., in consultation with Dr. Valentine, of Brooklyn.

The most rapid result was achieved in Case III., in consultation with Dr. S. Cohn of this city; laryngeal symptoms subsided in about twelve hours. The following cases were treated in the Municipal Hospital of Philadelphia, through the courtesy of Dr. Welch, physician in chief, and Dr. Bemis, house physician:

Case I.—F. N., two and a half years old, white, female, of Russian descent, had been ill a little longer than forty-eight hours when admitted to the hospital, October 2d. On admission the tonsils were large, inflamed, and covered with an extensive exudate, dark-gray in color, and the breath was fetid. There was also involvement of both nares. The glands of the neck were somewhat enlarged, and the color of the face was pale and sallow. The temperature was 100.2°; pulse, 124; the respirations, 24. Ten cubic centimetres of the antitoxine were injected at 6 P.M. (the day of admission). During the following twenty-four hours the temperature was recorded hourly, and varied between 99° and 101.4°; the pulse between 100 and 138 beats per minute; the respirations were from 16 to 28 The exudate in the fauces continued unchanged; there was free discharge from both nares; the greater part of the time this discharge consisted largely of blood. There was also oozing of blood from the mouth; the breath was fetid; the pallor was increasing and of a leaden hue. On November 4th the exudate in the fauces was unchanged; there was considerable epistaxis; the glands in the neck were enlarging; the temperature ranged from 98° to 100°; the pulse was 120; the respirations about 36. On November 5th the exudate in the fauces was not diminished; there was continued epistaxis; the breath was still fetid; the glands in the neck were even larger; there were some purpuric spots on the face; the color was very pale; prostration was great; the temperature ranged from 100.6° to 102.6°; the pulse was 140; the respirations, 28. At 1 P.M. of this day a dose of the stronger preparation of Aronson's antitoxine was injected by me. At 7 P.M. of the same day the condition of the patient was unchanged. For twenty-four hours after the first injection no other treatment was employed except the liberal use of milk and stimulants. Subsequently tincture of ferric chloride and mercuric chloride were given every two hours, and hydrogen dioxide applied locally every hour to the nares and fauces; strychnine sulphate, gr. $\frac{1}{100}$, was also given every six hours, continuing, of course, the free use of milk and whiskey.

On November 6th the exudate in the fauces was thinner, though still dark in color; blood was slowly dropping from the nose; the glands in the neck were somewhat diminished in size; the temperature, pulse, and respiration were unchanged. The pulse had considerable volume. Ex-

haustion had not increased, and the child took nourishment freely. On November 7th the exudate in the fauces had increased since the previous day, and a few small purpuric spots remained on the face. Epistaxis had ceased, though the nose was somewhat moist from blood. A large ecchymosis on the thigh appeared where the first dose of antitoxine was injected; the temperature was about the same, and the pulse was very weak indeed, just barely perceptible at the wrist, and could not be counted. The extremities were cold, the face pale and livid, and there was great drowsiness. The child was disinclined to take nourishment; there had been no bowel movement for twenty-four hours. Tinct. ferri chloridi and hydrarg. chlor. corrosiv. were continued every two hours, and hydrogen dioxide was applied to the throat. Strych. sulph., gr. $\frac{1}{100}$, every four hours, and whiskey and milk were ordered at short intervals. At 12 midnight, $\frac{1}{50}$ gr. strychnine sulph. was given hypodermatically.

On November 8th the exudate in the fauces had very much increased, covering not only the tonsils, uvula, and the anterior half-arches, but extending forward in front of the uvula. The exudate in the nares was also increasing; the glands in the neck were sensitive but not swollen. The temperature ranged between 97.6° and 99.8°; the pulse was just barely perceptible at the wrist; the heart's action was feeble, and the extremities were cold. In spite of this condition the child appeared bright and took milk fairly well. Strychnine sulph., gr. $\frac{1}{100}$, was ordered every three hours until two or three doses should be given.

At 5.20 A.M., 10 c.c. of Behring's antitoxine were injected. At 6.10 P.M., sulphuric ether ♏xv, was given hypodermatically, also at midnight gr. $\frac{1}{100}$ strychnine sulph. hypodermatically. On November 9th the exudate in the fauces was very much diminished; the heart's action was very weak, the pulse just perceptible at the wrist, but could not be counted. The temperature was about the same. The expression of the child was bright, but it took nourishment less willingly. There had been no bleeding from the nose for three days. Injections of strychnine were continued, gr. $\frac{1}{100}$ every four hours, and artificial heat was applied to extremities. At 2 P.M., 10 c.c. of Behring's antitoxine were again injected.

On November 10th there was still considerable exudate in the fauces and also in the nares; the heart's action was feeble, and the pulse at the wrist was still almost imperceptible; the extremities were cold, and the child took nourishment and stimulants somewhat reluctantly. Three hypodermatic injections of strychnine sulph. $\frac{1}{100}$ of a grain, were made in the last twenty-four hours. The child's expression, when awake, was quite bright. The heart-sounds were growing less and less audible, and death occurred at 10 P.M. from asthenia.

CASE II.—E. G. T., aged two years and eight months, white, female, born in Philadelphia, was admitted to the hospital October 2d, having a well-marked exudate on both tonsils and in one of the nasal cavities, of less than forty-eight hours' standing. At 6.10 P.M. on the day of admission 10 c.c. of Behring's antitoxine were injected. During the following twenty-four hours the temperature varied between 99° and 100.8°, being about the same as before the injection was administered; the pulse-rate was between 120 and 135; the respirations were from 20 to 30. The exudate on the tonsils seemed unchanged, as did that in the nose, except that the discharge from the nares was slightly less. On Novem-

ber 4th the exudate in the fauces and nares had neither extended nor diminished; the temperature was unchanged; the pulse-rate and respirations were about the same. On November 5th the exudate in the fauces and nares was unchanged, except that both nares were now involved; the glands in the neck were only very slightly swollen; the general condition of the child remained about the same as when the injection was given, with slight improvement. The child received the same internal and local treatment as the previous case, and took nourishment freely.

On November 6th there was but little change in the exudate in the fauces; the temperature had risen to 101.6°, and the rash of scarlatina had appeared. A sister of this child had developed scarlet fever two days previously. On November 7th the exudate was diminishing both in the fauces and nares; the temperature ranged between 100.8° and 101.8°; the pulse was 120. On November 8th the exudate in the fauces had disappeared; in the nose it was dry and much less distinct; the temperature was 101°. On November 9th there was no exudate in the fauces, and very little in the nose. The rash of scarlet fever was just barely characteristic. The child's general condition was much improved, and she had quite recovered from the diphtheria. The attack of scarlatina was very mild.

On November 12th gradual improvement was noted, and there was no exudate in the fauces, but there was still a very little in one nasal cavity. The temperature was about normal, and, from the time the scarlet fever began, it had not been higher than 101.8°. The pulse was 120. Desquamation commenced on this date. The child took nourishment well.

Case III.—A. J., thirteen years of age, colored, was admitted November 3d, having been ill four days. The exudate in the fauces covered the tonsils, the anterior half-arches, and the uvula completely. The temperature was 101.6°, the pulse 100, the respiration 28. There was only one very slight enlargement of the glands of the neck. There was no nasal involvement. Tinct. ferri chloridi and hydrarg. chlor. corros. were given internally every two hours, and hydrogen dioxide was applied locally every two hours. On November 4th the condition of the fauces remained unchanged; the temperature was 99.2°, the pulse 86, the respiration 25. A 1 per cent. solution of formalin was applied to the throat every two hours alternately with the hydrogen dioxide. On November 5th the exudate in the fauces remained the same; there was no increase of swelling of the glands of the neck; the temperature was 99°, the pulse 88, the respiration 20. There was very little exhaustion, and the child took nourishment well. At 1.10 P.M. I injected 10 c.c. of Behring's antitoxine (a bacteriologic examination was made by Dr. Kyle, and typical bacilli were found). Following this the temperature ranged between 100° and 106°. On November 6th the exudate in the fauces continued much the same, though somewhat thinner on the uvula. The temperature ranged from 98.4° and 98.8° to 100.8°; the pulse was about 90, the respiration about 20. The same internal and local treatment was continued; the child took nourishment and stimulants freely. On November 7th the exudate in the fauces had greatly diminished; the temperature was 99.4°, the pulse ranged from 80 to 90, the respiration was 18; nourishment was taken as usual, and the patient slept well. On November 8th the exudate was diminishing rapidly, the swelling of the

uvula was much less, and exhaustion was not great. On November 9th the exudate was much thinner and had disappeared in part, though considerable still remained. The same local and internal treatment was continued. The patient was now doing very well, and was placed on the regular house-diet.

On November 10th the general condition continued favorable; the fauces were quite free from exudate, but a little still remained on the uvula. Albumin continued in the urine in the same proportion.

On November 11th there was no exudate in the fauces except a little on the uvula; the temperature and pulse were about normal; the child took nourishment well, and strength was increasing. On November 12th there was a mere trace of exudation on the uvula; the temperature ranged between 98° and 100°; the pulse and respiration were about normal. The child was anxious to sit up.

Case IV.—B. M., white, male, aged five years, was admitted October 18th, on the third day of the disease. The exudate in the fauces was very great, covering the tonsils, the uvula, the anterior half-arches, and extending on the roof of the mouth in front of the uvula; there was also nasal involvement. The glands of the neck were enlarged. On October 19th the child was bleeding from the nose and mouth. On November 20th the exudate was unchanged, and there were croupy symptoms. On October 23d the general condition was about the same; the albumin on this date was about 60 per cent. of the bulk of the urine. The temperature had been running from 101° to 102°, the pulse from 100 to 118, the respiration from 22 to 26. On October 25th the exudate had diminished and epistaxis has ceased. The temperature was about 99°, the pulse 100, and the albumin was only 10 per cent. by bulk. On October 30th the fauces were almost free from exudate; no albumin was found in the urine; the temperature was about normal, sometimes subnormal; the pulse ranged from 96 to 100. There were marked evidences of toxemia; there was great pallor and weak heart-action. On November 5th the temperature had been ranging from 100° to 102.6°; there was no albumin in the urine; the pulse was from 98 to 112. There was a mere trace of exudate in the fauces, and still some nasal involvement; the pallor and prostration continued; there was a feeble pulse, and the cervical glands were still enlarged. There was an herpetic eruption on the lips. At 1.30 P.M. I injected 10 c.c. of Behring's antitoxine, the Klebs-Loeffler bacteria having been found to be present by Dr. Kyle. On November 9th the patient was gradually improving; the temperature was from 98.6° to 100°; the pulse from 90 to 120; no exudate existed in the fauces, and that in the nares was gradually growing less; the color was also improving, and the child took nourishment well. The general condition was much improved.

On November 12th the fauces were entirely free from exudate, and only a very little remained in the nares; the temperature was 98.6°. No albumin had been found in the urine for several days past. The child was constantly improving.

On November 15th no exudate could be seen in the fauces, but the nares had not quite assumed their normal appearance. The temperature and pulse were normal, and the appetite was good. The urine continued free from albumin. On November 19th the patient sat up a short while for the first time; the improvement continued, although the circulation was feeble and the pallor extreme. The fauces, with

the exception of marked redness, seemed healthy, but the nares were still somewhat abnormal. The appetite continued good, and the patient had apparently gained in weight. In this, as well as in the preceding cases, tincture of ferric chloride was continued three times daily, together with a nutritious diet.

On November 20th the child was somewhat indisposed, and the temperature was found to be 101°. During the two preceding days the patient had been sitting up.

On November 21st a rubelloid rash covering the trunk and extremities appeared. The temperature fell to normal, or nearly so, and the appetite was as usual. There were no catarrhal symptoms.

On November 23d the temperature continued normal, and the rash had entirely disappeared, without leaving the mottled condition of the skin peculiar to measles; hence the diagnosis of that disease must be excluded. There was no albumin in the urine, but there was slight evidence of paralysis.

Case V.—A white male, eight years of age, was admitted November 9th, having been ill seven days. The exudate in the fauces covered the tonsils, the anterior half-arches, and the uvula, and extended a short distance on the roof of the mouth in front of the uvula; both nares were also involved. The breath was offensive; the glands on both sides of the neck were considerably enlarged, and the skin over the swollen glands was red. The temperature was 102.8°, the pulse 136, the respiration 36. Ten c.c. of Behring's antitoxine were injected under the skin on the back at 12 o'clock M. by me. The patient was at this time taking internally about 6 minims tinct. ferri chlorid. and $\frac{1}{32}$ gr. of mercuric chloride every two hours; locally, hydrogen dioxide undiluted, alternately with a one per cent. solution of formalin, was applied every hour, whiskey ʒij every two hours, and milk *ad libitum*. On November 10th the temperature was 100°, the pulse 120, the respiration 32. The exudate in the fauces remained about the same, except that it presented the appearance of peeling off in some places; in the nares the exudate was unchanged; the glandular swelling also remained about the same. The child at times was drowsy, and at other times restless.

On November 11th the exudate in the fauces and nares remained about the same; it was still dark in color and the breath was offensive. The glandular swelling had not increased. The temperature was about 100°, the pulse 128, the respiration 32. Albumin was found in the urine in the proportion of about one-tenth part of the bulk of the urine. The child took nourishment well.

On November 12th there was very little, if any, change in the exudate in the fauces and nares; at times there was slight epistaxis. The temperature was 99.8°, the pulse 116, the respiration 26. There was no increase of the glandular enlargement; exhaustion was not great; and the child continued to take nourishment and to rest well.

On November 13th the exudate in the fauces was somewhat thinner, and that in the nares also seemed to be slightly diminished. The temperature ranged between 98.4° and 99.6° F.; the pulse was more feeble, but the respirations were unchanged. Nourishment was taken, though somewhat reluctantly, and vomiting occurred once or twice. The heart's action was weak and the extremities were growing cold. Strychnine sulphate was ordered in doses of gr. $\frac{1}{100}$ every four hours, and the whiskey was increased. On November 14th the exudate in

the fauces had diminished still further; the pulse ranged from 96 to 104, and was almost imperceptible at the wrist; the respirations ranged from 20 to 30; the temperature ranged from 98° to 98.4°. Albumin was found to be present in the urine (about 2 per cent. by bulk). The extremities were constantly growing colder; vomiting was occurring occasionally; the child took nourishment and medicines more reluctantly; the pallor of the face was increasing, and the patient was rapidly losing strength. Spiritus ammonii aromaticus in fʒss doses was ordered every half hour, and strychnine sulphate, gr. $\frac{1}{100}$, hypodermatically, every four hours. The exhaustion progressively increased, and death occurred from toxemia at 10 o'clock P.M.

In conclusion I desire to say that many of my cases not reported are from private families who begged me not to publish them; from several other cases my detailed reports are lacking—these will be published later.

To sum up: I have injected in all 34 cases; of these 29 were malignant cases, in which a grave prognosis was given by the attending physician or by myself in consultation; 4 were mild cases in the commencement of the disease, and one case was moribund.

By *malignant* I mean cases that had either distinct evidence of sepsis, showing low temperatures or very high temperatures, and where marked somnolence was evident, where cervical glands were considerably enlarged, and where at times the skin showed, in addition to cold, clammy perspiration, a decided icteric appearance; where there was also a foul mouth, a distinct cadaveric breath, and where only a grave prognosis was given. Such cases not only showed pharynx, tonsils, and uvula involved, but also symptoms of stenosis of the larynx and occlusion of the nares.

By *mild* I mean such cases as were seen on the first few days of illness, where the membranes were limited to either small areas of the pharynx, tonsils, or uvula, and where no complications of larynx and nares were observed. Mild cases were also those in which small quantities of albumin in the urine were noticed, and where no pulmonary or distinct nephritic complications could be diagnosticated.

The moribund case referred to was the one seen in consultation with Dr. Welch at the Municipal Hospital of Philadelphia, and the child not only was pulseless, but had cold extremities and showed marked evidence of general septicæmia. Still it lingered a number of days, showing the influence of the strong Aronson serum in neutralizing the toxic elements.

I have had 34 cases—30 malignant and 4 mild—32 of which recovered. I have 32 cures and 2 deaths—in all 34 cases treated, or a mortality of 5.8 per cent.

These cases were not selected, for some were poorly nourished, some in excellent vitality, with careful nursing, good hygiene. The main point was to apply the antitoxine as early as possible, and counteract the septic matter absorbed, and thereby avoid complications, besides

using the local treatment of swabbing the throat with a 1 : 2000 bichloride of mercury solution, using a fresh swab for each application, and burning the same immediately after using it.

The technique of injection is simple. Having properly sterilized the syringe by boiling and using 0.5 per cent. tricresol, I commence by injecting 10 c.c. in mild cases, and 20 c.c. in malignant cases, by pinching a fold of the skin in the intra-scapular region, and allowing the serum to be slowly injected. I believe it proper, however, to have a syringe of suitable size and inject the required amount, rather than inject several places. The calibre of the latter must necessarily be quite large, owing to the thickness of the serum, which is at times rather mucilaginous. It is proper to note all differences and effects on the false membrane and the swelling of the glands, the behavior of the temperature, the condition of the urine, the effect on the heart, and especially the pulse.

There should be no hesitation in injecting on the second day, and, if no effect is seen, repeating the injection on the third day, as there is absolutely no risk from the injection. It is a perfectly safe remedy, and shows no immediate reaction. It differs from tuberculin and vaccine in that it causes no reaction. A case of antitoxine treatment will show no symptoms directly attributable to the remedy, unless it be in some cases urticaria. The temperature does not fall by crisis, but by lysis, with antitoxine treatment. Massage of the serum after the injection should not be practised, according to Heubner, Aronson, Baginsky, and others.

Let us not lose sight of the fact that in the use of this new agent we are treating diphtheria, and that all discharges, be they from the nose, throat, or mouth, and possibly feces and other excrements, should be subjected to a rigid disinfection. This, if possible, before leaving the body. For this purpose local swabbing of all visible membranes with a 1 : 2000 bichloride of mercury solution, using glass rods with absorbent cotton—the latter to be burned immediately after swabbing; the glass rod to be put into bichloride solution. We still require most thorough naso-pharyngeal antisepsis for this purpose, lukewarm (105° to 110° F.) normal table-salt solution, injecting either nostril until the stream flows out of the other side, using considerable force at times. Great attention must be paid to the recumbent posture, which has been so strongly advocated in Berlin, especially so where the patient's heart is weak from diphtheritic poison, and the child is douched while flat on its back, with a rubber sheet around its arms and neck to prevent useless struggling, so well known in the former method of syringing in the sitting posture. One nostril only need be irrigated until the saline solution flows out of the other side.

Stimulation should be cautiously followed out. It should be used where there is weakness of pulse and where the heart's action is slowed

—then, however, it should be freely administered; good Tokay, and Baginsky advises Greek wines (Mavrodaphne), and other kinds. These latter wines, being sweet, are very greedily taken by children. Neither the ice-collar nor any other form of external local application was used in my experience abroad or in this country with the serotherapy.

187 Second Avenue, New York.